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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/272,809	03/19/1999	JOHN CLARK LAGARIAS	23070-943	6118

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/272,809	LAGARIAS, JOHN CLARK	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7-19 and 21-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5, 7-19 and 21-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed October 3, 2005 has been entered. Claims 5, 17, and 24 have been cancelled. Claims 2, 6 and 20-21 have been cancelled. Claims 1, 3-5, 7-19 and 22-32 are under consideration in this office action.

Withdrawal of Objections and Rejections

2. The following objections and rejections have been withdrawn in applicants' amendments and arguments:

a) The objection of claims 5, 6,17, 21 and 24 under 37 CFR 1.75(c); and

b) The double patenting rejection of claims 1,3,9-21 and 27-31 under the judicially created doctrine of obviousness-type double patenting.

New Grounds of Objection and Rejection

Claim Objections

3. Claim 24 is objected to because of the following informalities: Claim 24 recites "is a shown" instead of "is as shown. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Clack et al. The claims are drawn to a composition comprising an apoprotein polypeptide of between about 190 amino acids and about 400 amino acids, which comprise a lyase domain wherein the polypeptide is selected from a plant apoprotein.

Clack et al., teach the sequence and expression of phytochrome apoproteins from the *Arabidopsis* plant. All of the detectable phytochrome apoprotein genes have been isolated and sequenced (page 414). Figures 3A and 3B show the derived amino acid sequence of the PHYD and PHYE genes. Figure 4 shows a plot of amino acid residues for five apoproteins, PHY A-E. The apoprotein of Clack et al., has 100% sequence identity to SEQ ID NO:9 of the instant claims.

Thus the apoprotein polypeptide taught by Clack et al., comprises a plant apoprotein polypeptide comprising about 190 to 400 amino acids and a lyase domain.

5. Claims 1, 3-4 and 7-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaneko et al. The claims are drawn to a composition comprising an apoprotein polypeptide of between about 190 amino acids and about 400 amino acids, which comprise a lyase domain and the polypeptide is selected from a plant apoprotein.

Kaneko et al., teach the sequence analysis from unicellular cyanobacteria

Synechoystis species. Kaneko et al., disclose the sequencing strategy. Kaneko et al., teach 1276 amino acid polypeptide having 100% identity to SEQ ID NO:2.

Thus the cyanobacterium comprises the apoprotein polypeptide and the lyase domain just as required by the instant claims.

6. Claims 1,7 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Yeh et al. The claims are drawn to a composition comprising a *Synechocystis* apoprotein polypeptide of between about 190 amino acids and about 400 amino acids, which comprise a lyase domain and the polypeptide is selected from a plant apoprotein wherein the apoprotein is covalently linked to a phycoerythobilin to form a fluorescent adduct.

Yeh et al., teach a cyanobacterial phytochrome two-component sensory system. The *Synechocystis* species produced the phytochrome named cph1 that has a lyase domain (page 1505). The art teaches affinity tagged versions of the apoproteins (page 1505). The Cph1 is a functional phytochrome apoprotein that has the ability to catalyze its own chromophore attachment to yield photoreversible adducts with higher plant phytochromobilin and its phycobilin analog (page 1505). Also taught is the assembly with phycoerythrobilin, a phycobilin analog which also produces a visualizable covalent adduct (page 1505).

Thus Yeh et al., teach a composition comprising a *Synechocystis* apoprotein which is covalently linked to a bilin to form a fluorescent adduct.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeh et al., in view of Stryer et al., (US Patent 4,859,582). The claims are drawn to a composition comprising a *Synechocystis* apoprotein polypeptide of between about 190 amino acids and about 400 amino acids, which comprise a lyase domain and the polypeptide is selected from a plant apoprotein wherein the apoprotein is covalently linked to a fluorescent adduct which is further linked to a biomolecule.

Yeh et al., has been discussed above, however Yeh et al., do not disclose a fluorescent adduct further linked to a biomolecule.

Stryer et al., teach fluorescent conjugates for analysis of molecules and cells. Stryer et al., teach composition comprising phycobiliproteins conjugated to a member of a specific binding pair (col. 2, lines 49-52). The biliproteins can be linked to any ligand of interest (col.3, lines 33-35). The ligand can be any compound of interest including polypeptides, immunoglobulins or antibodies (col. 3, lines 38-68). The structures of phycobiliproteins have been studied and their fluorescent spectral properties are well known (col. 4-5, lines 68-2).

Therefore, it would have been prima facie obvious at the time of applicants' invention to modify the composition of Yeh et al., which comprises an plant apoprotein polypeptide having a lyase domain wherein the apoprotein is covalently linked to a fluorescent adduct wherein the modification is that the composition is further linked to a biomolecule, as taught by Stryer et al. No more than routine skill would have been required to combine the two compositions each of which is taught by the prior art to be useful for the purpose of detection, in order to form a third composition to be used for that same detection purpose. One would have a reasonable expectation of success since the idea of combining the two flows logically from their having been individually taught in the prior art.

8. Claims 17-19, 22-23, 25, 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stryer et al., (US Patent 4,859,582) in view of Yeh et al. The claims are drawn to a method of detecting the presence of a biomolecule in a sample comprising providing a sample comprising a biomolecule is linked to the fluorescent adduct consisting of a bilin and apoprotein; contacting the sample with light and detecting the emitted light. The dependant claims are drawn to the specific wavelengths, characteristics of the apoprotein, bilin and biomolecule.

Stryer et al., teach fluorescent conjugates for analysis of molecules and cells. Stryer et al., teach a wide variety of methods involving binding of ligand to receptors for detection, analysis or measurement of the presence of the ligand or receptor (col. 2, lines 55-59). The biliproteins can be linked to the ligand of

interest (col.3, lines 33-35). The ligand can be any compound of interest including polypeptides, immunoglobulins or antibodies (col. 3, lines 38-68). The structures of phycobiliproteins have been studied and their fluorescent spectral properties are well known (col. 4-5, lines 68-2). For instance, the bilins are visible at wavelengths between 550nm and 650nm, see Table 1; thereby teaching detection at the instantly claimed wavelengths. Furthermore, the biliproteins can be used in immunoassays where the biliprotein serves as a fluorescent label and is conjugated to either a ligand or receptor for detection (col. 5-6, lines 66-15). Example 9 teaches the sample with fluorescent adduct complex, and detecting a fluorescent signal at 576nm. However Stryer et al., do not teach the use and linkage of an apoprotein.

Yeh et al., has been discussed above, as teaching an apoprotein polypeptide of between about 190 amino acids and about 400 amino acids, which comprise a lyase domain wherein the polypeptide is selected from a plant apoprotein and the apoprotein is covalently linked to a phycoerythobilin to form a fluorescent adduct.

Therefore, it would have been prima facie obvious at the time of applicants' invention to modify the method of Stryer et al., to include the apoprotein of Yeh et al., which comprises an plant apoprotein polypeptide having a lyase domain wherein the apoprotein is covalently linked to a fluorescent adduct. No more than routine skill would have been required to combine the two products each of which is taught by the prior art to be useful in a method of detection, in order to form a third composition to be used within a method of

detection. One would have a reasonable expectation of success since the idea of detecting the presence of a molecule in a sample comprising an a fluorescent adduct linked to a biomoleucle is already well known in the art, along with the idea of using a two-component light sensory system and the idea of combing them logically flows from their having been individually taught in the prior art.

9. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stryer et al., (US Patent 4,859,582) and Yeh et al., further in view of Clack et al. The claims are drawn to a method of detecting the presence of a biomolecule in a sample comprising providing a sample comprising a biomolecule linked to the fluorescent adduct comprising an apoprotein having SEQ ID NO:9; contacting the sample with light and detecting the emitted light.

Stryer et al., Yeh et al., and Clack et al., have been discussed above. Stryer et al., taught a method of detecting the presence of a biomolecule, however Stryer et al., did not teach SEQ ID NO:9. Yeh et al., teach an apoprotein linked to a fluorescent adduct. Clack et al., taught SEQ ID NO :9.

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the method of Stryer et al., and Yeh et al, to include the apoprotein of Clack et al., which comprises a plant apoprotein polypeptide having SEQ ID NO:9. No more than routine skill would have been required to exchange the apoprotein of Yeh et al., for the apoprotein of Clack et al., since the apoproteins are known to link to fluorescent adducts and be detectable within methods of detection. Moreover, one would have a reasonable expectation of

success since the idea of detecting the presence of a molecule in a sample comprising a fluorescent adduct linked to a biomoleucle is already well known in the art along with the idea of using a two-component light sensory system and the idea of combing them logically flows from their having been individually taught in the prior art.

10. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stryer et al., (US Patent 4,859,582) and Yeh et al., further in view of Kaneko et al. The claims are drawn to a method of detecting the presence of a biomolecule in a sample comprising providing a sample comprising a biomolecule linked to the fluorescent adduct comprising an apoprotein having SEQ ID NO:2; contacting the sample with light and detecting the emitted light.

Stryer et al., Yeh et al., and Kaneko et al., have been discussed above. Stryer et al., taught a method of detecting the presence of a biomolecule, however Stryer et al., did not teach SEQ ID NO:2. Yeh et al., teach an apoprotein linked to a fluorescent adduct. Kaneko et al., teach Cph2 also known as SEQ ID NO:2.

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the method of Stryer et al., and Yeh et al, to include the apoprotein of Kaneko et al., which comprises a plant apoprotein polypeptide having SEQ ID NO:9. No more than routine skill would have been required to exchange the apoprotein of Yeh et al., for the apoprotein of Kaneko et al., since the apoproteins are known to link to fluorescent adducts and be detectable within

methods of detection. Moreover, one would have a reasonable expectation of success since the idea of detecting the presence of a molecule in a sample comprising a fluorescent adduct linked to a biomoleucle is already well known in the art along with the idea of using a two-component light sensory system and the idea of combing them logically flows from their having been individually taught in the prior art.

Prior Art

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Hill et al., teach the expression of phytochrome apoprotein from the oat plant *Avena sativa* and the formation of photoactive chromoproteins by assembling them with phycocyanobilin.

Conclusion

12. No claims allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
January 17, 2006

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